IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Ira Sanders	**Examiner:**	Rodney Swartz
Application No.:	10/535,504	**Confirmation No.:**	9381
Filed:	May 18, 2005	**Group Art Unit:**	1645
Title:	TREATMENT OF MAMMALIAN REACTION OF IGE INTERACTIONS		

Attorney Docket No.: 21864-4

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

August 4, 2009

Declaration of Dr. Ira Sanders

I, the undersigned, hereby declare and state that:

1. I received a degree in medicine from Creighton University College of medicine. I have engaged in research related to neurotoxins since 1989. My curriculum vitae is attached as Exhibit A.

2. I am the inventor of the subject matter described and claimed in the above referenced application entitled *Treatment of Mammalian Reaction of IGE Interactions*, filed on May 18, 2008 (the "Application"), which has published as Publication No. US 2006/0008462. I am aware that the Application claims priority to a provisional filing date of Nov. 21, 2002.

3. I have reviewed the Final Office Action mailed February 4, 2009 (the "Action"). In the Action, the Examiner rejected claims 1-3, 8, 11-13, 15 and 16 of the application as being anticipated by WO 95/28171 (the '171 Application) of which I am a named inventor. I

understand that the Examiner takes the position that "[s]ince the scope of the claims is drawn to a method of blocking or reducing physiological reactions and not to actual blocking of IGE antibodies binding with antigen, [the reference teaches] the claimed methods in that the reference teaches controlling at least one symptom of rhinorrhea, otitis media, excessive salivation, asthma, COPD, excessive stomach secretion, spastic colitis or excessive sweating in mammals, including humans.."

4. I participated in the Interview with the Examiner on April 7, 2009 and have reviewed the Interview Summary wherein the Examiner stated that "[l]isting of specific allergic conditions not taught by the prior art of record may obviate the 102(b) rejection, but still may be rejected under 103(a) if the mechanisms of disease conditions of the instant claims are sufficiently similar to those taught by the prior art." The Examiner further stated that "recitation of unique administration methods may also obviate the remaining rejections."

5. I am aware that the present claims of the Application have been amended in order to be directed to allergic rhinitis (claim 1) and allergic dermatitis (claim 25).

6. Allergic rhinitis and allergic dermatitis are not taught by the '171 Application, nor do these conditions have a similar mechanism of action as conditions in the '171 Application.

7. The '171 Application is directed to treating the condition of vasomotor rhinitis (see, e.g., page 2, lines 8-11; lines 33-35; page 14, lines 2-4 of the '171 Application) which is a distinct condition from allergic rhinitis as recited in the present claims.

8. Vasomotor rhinitis is a simple and relatively uncommon condition believed caused by overactivity of cholinergic nerves innervating a subset of nasal glands to produce a thin watery secretion. As stated in an authoritative source, "...vasomotor rhinitis occurs in some elderly people who experience a dripping, watery rhinorrhea that becomes pronounced at

mealtime but may be persistently present in many daily activities. There is little sneezing, pruritis, congestion, or lower respiratory tract symptoms associated with this entity. Eosinophils are not present in nasal secretions. Treatment with most medications including antihistamine/decongestants, cromolyn sodium, and topical steroids are usually not effective..."[1]

9. In sharp contrast, allergic rhinitis is caused by a distinct mechanism from that of vasomotor rhinitis. The primary source of fluid in allergic rhinitis is from vasodilation and increased permeability of nasal blood vessels. This allows fluid to "leak" directly from blood vessels into the nasal cavity. A secondary mechanism is that the neurohumors released from immune cells directly stimulate mucous secreting cells.

10. Vasomotor rhinitis is limited to a watery rhinorrhea and caused by eating or temperature change (see page 11, lines 18-22 of the present application). In contrast to vasomotor rhinitis, allergic rhinitis is associated with:

(i) the release of histamine, heparin and neuropeptides which in turn cause vessels to dilate and congest the nose, or bypass nerves to directly stimulate mucus production as well as cause reflex mucus production, increased cilia movement, nasal congestion and sneezing (see page 9, lines 10-14 of the present application);

(ii) mast cell degranulation with reflex mucous production, increased cilia movement and sneezing (see page 7, line 30 to page 8, line 2 of the present application);

(iii) the release of nerve growth factor from mast cells and eosinophils, thereby resulting in growth of nasal sensory nerves and increased hyperactivity which makes the patient more susceptible to viral and bacterial infections. In addition allergies cause

[1] Immunology and Allergy Clinics of North America, Fahey J and Fauci A, eds. Volume 7, Issue 1, Upper Respiratory Disorders, chapter, NonAllergic Chronic Rhinitis Syndromes, Jocobs, R, pages 93-104.

qualitative changes in nerve reflexes such that they are activated more easily by both allergic and non-allergic stimuli (see page 8, lines 10-21 of the present application).

11. To further evidence the distinct mechanisms of vasomotor rhinitis and allergic rhinitis, I note that vasomotor rhinitis is treated with drugs that block acetylcholine, while allergic rhinitis is treated with desensitization, anti-histamines and steroids. The drugs used for allergic rhinitis are not therapeutically effective on vasomotor rhinitis (as paragraph 8 above). This is because the mechanism of vasomotor rhinitis appears to involve only a small group of cholinergic nerves innervating the nasal glands that produce a watery secretion with low content of mucus. In contrast, allergic rhinitis involves many different cell types including B-cells, T-cellls, macrophages, basophils, mast cells, eosinophils, as well as sensory and non-cholinergic nerves. The mediators that are involved in allergic rhinitis are extremely varied and include: histamine, tryptase, chymase, kinins, heparin, leukotrienes, prostaglandins, eosinophilic basic protein, nerve growth factor and many others.

12. In contrast to the treatment of vasomotor rhinitis, treatment of allergic rhinitis according to the present claims presents the following properties:

-decreased release of histamine, heparin and neuropeptides;

-decreased rhinorrhea from permeable nasal blood vessels, from direct stimulation of mucus glands by neurohumors, and from reflex mucus production;

-decreased nasal congestion and sneezing.

13. The '171 Application is specific to the nerves that use acetylcholine as their neurotransmitter, and the possibility of blocking other neurotransmitters or neuropeptides is rejected by the interpretation therein of the prior scientific literature (see page 2, lines 25-29 of the '171 Application), the results of the salivation experiment described in the specification (see

page 11, line 26-29 of the '171 Application), as well as the rhinorrhea experiments (see page 18 line 25-28 and page 19, lines 17 to 21 of the '171 Application).

14. The term "rhinorrhea" means excess nasal secretion and the term is applied to a variety of other conditions. For example, cerebrospinal fluid (CSF) rhinorrhea occurs when there is a skull fracture and CSF leaks from the central nervous system out of the nose. Another example is the purulent (pus) rhinorrhea resulting from an acute sinus infection. In view of the disclosure of the treatment of vasomotor rhinorrhea in the '171 Application, it is my opinion that no practitioner of ordinary skill in the art would generalize that any rhinorrhea such as CNS rhinorrhea or purulent rhinorrhea could be blocked by neurotoxins. Similarly, it is my opinion that in view of the '171 Application, a practitioner of ordinary skill in the art would not have any expectation of success that allergic rhinorrhea could be blocked by neurotoxins as recited in the present claims.

15. To further evidence the distinct mechanisms of vasomotor rhinitis and allergic rhinitis, I note that the only surgical treatment for vasomotor rhinitis is to cut the nerves innervating the nose (Vidian neurectomy). This is never done and would not be effective for allergic rhinitis. Rather, surgeries for allergic rhinitis treat the long term changes of mucosal thickening, nasal polyps and recurring sinus infections.

16. Allergic dermatitis is also caused by allergic pathways as discussed above and in my opinion, independent claim 26 directed to treating allergic dermatitis is also not anticipated or obvious from the '171 Application.

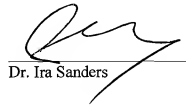
17. Further independent claim 27 incorporates the unique administration methods of claims 6, 7, 9, 10, 14, 18-20 and 25 which were not included in the prior art rejections in the

February 4, 2009 Office Action. It is my opinion that these claims are also not obvious in view of the '171 Application due to the recitation of the administration methods.

18. For the reasons set forth above in paragraphs 1-17, it is my opinion that the present claims of the Application would not be anticipated or obviated by the '171 Application.

19. I hereby declare further that all statements made herein by our own knowledge are true and that all statements made on information and belief are believed to be true and further that we make these statements with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application of any patent issuing therein.

Signed this 4th day of August, 2009



Dr. Ira Sanders